RVD2008-27

Re-evaluation Decision

Trichlorfon

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Overview

Re-evaluation Decision for Trichlorfon

After a re-evaluation of the insecticide trichlorfon, Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is granting continued registration of some uses of trichlorfon in Canada and phasing out the uses with risk concerns.

An evaluation of available scientific information found that, under the revised conditions of use, certain uses of products containing trichlorfon that do not involve a level of concern to human health or the environment have value in the food and crop industry. These uses include ground application on Balsam fir and spruce trees in farm woodlots, rights-of way and Christmas tree plantations as well as uses on beef and non-lactating dairy cattle. As a condition of the continued registration for these particular uses, new risk-reduction measures must be included on the labels of all products. Certain uses of trichlorfon are to be phased-out because of the human health risks and/or risks to the environment. These are using trichlorfon in municipal parks and on outdoor ornamentals as well as applying trichlorfon by air. In addition, registrants must submit additional scientific information.

The regulatory approach for the re-evaluation of trichlorfon was first presented in the Re-evaluation Note REV2007-05, *Preliminary Risk Assessment of Trichlorfon* and the Proposed Re-evaluation Decision PRVD2008-14, *Trichlorfon*.[1] This Re-evaluation Decision[2] describes this stage of PMRA's regulatory process for the re-evaluation of trichlorfon as well as summarizes the Agency's decision and the reasons for it. No comments were received during either of the consultation processes. This decision is consistent with the proposed re-evaluation decision stated in PRVD2008-14, *Trichlorfon*. To comply with this decision, registrants of products containing trichlorfon will be informed of the specific requirements affecting their product registration(s) and of regulatory options available to them.

For more details on the information presented in this Re-evaluation Decision, please refer to the Science Evaluation in the related Proposed Re-evaluation Decision PRVD2008-14, *Trichlorfon*.

What Does Health Canada Consider When Making a Re-evaluation Decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable if there is reasonable certainty that no harm to human health, future generations or the environment will result from use or exposure to the product under its

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1 "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

2 "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

conditions or proposed conditions of registration.[3] The Act also requires that products have value[4] when used according to the label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

To reach its decisions, the PMRA applies rigorous, modern hazard and risk assessment methods and policies. These methods consider the unique characteristics of sensitive populations in humans (e.g. children) and organisms in the environment (e.g. those most sensitive to environmental contaminants). These methods and policies also consider the nature of the effects observed and the uncertainties present when predicting the impact of pesticides. For more information on how the PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the PMRA's website at www.pmra-arla.gc.ca.

What Is Trichlorfon?

Trichlorfon is a broad spectrum, Resistance Management Group 1B (organophosphate) insecticide that inhibits the enzyme acetylcholinesterase and interrupts the transmission of nerve impulses. It works by contact and ingestion action. Products containing trichlorfon are registered under the following use-site categories: Forest and Woodlots, Livestock for Food, Terrestrial Food Crops, Terrestrial Feed Crops, Ornamentals Outdoors, Greenhouse Food Crops, Industrial Oil Seed and Fibre Crops, Structural, and Human Habitat and Recreational Areas.

Following the re-evaluation announcement for trichlorfon, Bayer CropScience Inc., the registrant of the technical grade active ingredient, indicated it intended to discontinue all uses except for those on Balsam fir and spruce trees in farm woodlots, rights-of way, Christmas tree plantations and municipal parks, on beef and non-lactating dairy cattle and on ornamentals. Only uses the registrant supported were considered in the health and environmental risk assessments of trichlorfon.

Health Considerations

Can Approved Uses of Trichlorfon Affect Human Health?

Trichlorfon is unlikely to affect your health when used according to the revised label directions.

Exposure to trichlorfon may occur through diet (food and water), by mixing, loading or applying the pesticide, or when entering a treated site. The PMRA considers two key factors when assessing health risks: the dose levels at which no health effects occur and

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3 "Acceptable risks" as defined by subsection 2(2) of the *Pest Control Products Act*.

4 "Value" as defined by subsection 2(1) of the *Pest Control Products Act*: "the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product's (a) efficacy; (b) effect on host organisms in connection with which it is intended to be used; and (c) health, safety and environmental benefits and social and economic impact."

the dose levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (e.g. children and nursing mothers). Only those uses where exposure is well below levels that cause no effects in animal testing are considered acceptable for continued registration.

Trichlorfon is highly to moderately toxic via the oral route and of low toxicity via the dermal and inhalation routes of exposure. Trichlorfon is moderately irritating to eyes, non-irritating to skin and is considered a skin sensitizer.

Following oral exposure, trichlorfon is readily absorbed and rapidly eliminated with little accumulation in the tissues. Exposure to trichlorfon in adult animals produced inhibition of acetylcholinesterase, progressing to clinical signs at higher doses. Effects on pup development, including transient behavioural changes and brain-weight effects, have been observed at doses resulting in maternal toxicity. Several studies from the published literature have also raised concerns regarding the neurotoxic effects of trichlorfon on prenatal brain development in guinea pigs and pigs.

In the environment, trichlorfon degrades to dichlorvos, which is also an organophosphate. Dichlorvos is also a mammalian metabolite and is a more potent acetylcholinesterase inhibitor than trichlorfon. Thus, the risk assessment took dichlorvos into consideration. Acetylcholinesterase is an enzyme responsible for the proper functioning of the nervous system and is inhibited following an overexposure via oral, dermal or inhalation routes. Symptoms including tremors, salivation, diarrhea and shortness of breath may occur in animals and humans.

The human data on trichlorfon indicate that acute exposure to high doses of trichlorfon results in those effects typically associated with acute organophosphate intoxication. Trichlorfon has been shown to cause neuropathology in hens and humans directly exposed. The occurrence of neuropathy in humans with low-level exposure heightens the concern for this compound, particularly because the neuropathy is of a persistent enough nature to render severe consequences in a subpopulation of aged individuals.

As some concerns were noted with the current use pattern for trichlorfon, the PMRA is requiring the phase out of uses in municipal parks and is requiring further protective measures, such as product use changes, protective equipment and improved work practices, to further reduce the level of human exposure to trichlorfon. In addition, specific toxicity information regarding symptoms of overexposure are required in the Toxicological Information section of the product labels.

Risks in Residential and Other Non-Occupational Environments

Residential risks are of concern. Therefore, residential uses are to be phased-out.

Exposure may occur after trichlorfon is used in outdoor residential and recreational areas. Given trichlorfon degrades to dichlorvos, adults and children can be exposed to both when entering a treated site. Adults and children could experience short-term exposure

when or immediately after it is used, for example people walking in treated municipal parks. There are insufficient data to estimate residues of trichlorfon and dichlorvos in municipal parks. It was assumed the exposure of hikers would be similar to scouters entering a treated forest. Based on this re-entry activity, the risk estimates associated with the residential uses do not meet current standards. Toddlers are expected to experience greater exposure to trichlorfon than adults after the product is applied because the activities associated with toddlers are considered more intensive. As well, these estimates do not include potential inhalation exposure to dichlorvos. Currently, no data are available to estimate the concentration of dichlorvos in the air after trichlorfon is applied on to spruce and fir trees in municipal parks.

As restricted-entry intervals calculated for adults are not considered feasible for municipal parks, a postapplication assessment for children was not pursued. Children's exposure is expected to be higher. Consequently, the PMRA is requiring the phase-out of uses in residential settings such as municipal parks.

Occupational Risks From Handling Trichlorfon

Exposure risks for mixers, loaders and applicators are not of concern provided additional risk-reduction measures are observed.

Workers can be exposed to trichlorfon when mixing, loading or applying the pesticide. Worker exposure estimates are based on the best available data at this time. The assessment may be refined with exposure data that are more representative of modern application equipment and engineering controls. Biological monitoring data could also further refine the assessment. No specific handler exposure data were submitted for trichlorfon. Therefore, dermal and inhalation exposures were estimated using data from the Pesticide Handlers Exposure Database (PHED), Version 1.1.

The risk estimates associated with mixing, loading and applying activities for current label uses meet current standards and are not of concern, provided engineering controls and/or personal protective equipment are used.

Postapplication risks are of concern for workers performing high exposure activities.

As trichlorfon degrades to dichlorvos, workers can be exposed to both when entering a treated site to conduct activities such as handling treated ornamentals and Christmas trees, or when handling treated livestock. The postapplication occupational risk assessment considered exposures to workers entering treated sites, including forests, nurseries and Christmas tree plantations. It is expected that exposure of livestock handlers would be less than that of individuals applying product. Therefore, a quantitative postapplication exposure assessment was not conducted. However, mitigation measures are recommended to protect people handling treated animals.

Restricted-entry intervals are calculated to determine the minimum length of time required before workers or others can safely enter a treated site. An restricted-entry intervals is the amount of time that must elapse before residues on surfaces or in air decline to a level at which performing a specific activity results in acceptable exposures.

The length of time it takes for trichlorfon and dichlorvos residues to reach acceptable levels is not considered feasible for all uses; therefore, the PMRA is requiring that uses on outdoor ornamentals be phased out.

Residues in Water and Food

Dietary risks from food and water are not of concern.

Reference doses define levels to which an individual can be exposed over a single day (acute) or lifetime (chronic) and expect no adverse health effects. Generally, dietary exposure from food and water is acceptable if it is less than 100% of the acute reference dose or chronic reference dose (acceptable daily intake). An acceptable daily intake is an estimate of the level of daily exposure to a pesticide residue that, over a lifetime, is believed to have no significant harmful effects.

Acute and chronic dietary exposure to trichlorfon was estimated using anticipated residue data from dermal application studies with livestock. The use on livestock is the only supported food use of trichlorfon. The acute potential daily intake of trichlorfon accounts for 1.3% (99.9th percentile) of the acute reference dose for the general population, and 2.1% of the acute reference dose for the highest exposed population group, children three to five years of age. The chronic dietary exposure as a percentage of the acceptable daily intake is 7% for the general population and 13% for the highest exposed population groups, children one to two and three to five years of age. Therefore, the acute and chronic dietary risk from trichlorfon is not considered to be of concern.

The supported uses of trichlorfon are not expected to result in any significant drinking water exposure. Therefore, drinking water risks are not of concern.

The *Food and Drugs Act* prohibits the sale of food containing a pesticide residue that exceeds the established maximum residue limit (MRL). Pesticide MRLs are established for *Food and Drugs Act* purposes through the evaluation of scientific data under the *Pest Control Products Act.* Each MRL value defines the maximum concentration in parts per million (ppm) of a pesticide allowed in/on certain foods. Food containing a pesticide residue that does not exceed the established MRL does not pose an unacceptable health risk.

Currently, there is no definition for the residue of concern for trichlorfon, and no MRLs are specified. The supported food uses of trichlorfon are on beef cattle and non-lactating dairy cattle. Where no specific MRL is established for a pest control product, subsection B.15.002(1)(a) of the Food and Drug Regulations applies. This requires that residues do not exceed 0.1 ppm, which is considered a general MRL for enforcement purposes.

However, changes to this general MRL may be implemented in the future, as indicated in Discussion Document DIS2006-01, *Revocation of 0.1 ppm as a General Maximum Residue Limit for Food Pesticide Residues [Regulation B.15.002(1)]*. A transition strategy will be established to allow permanent MRLs to be promulgated prior to the revocation of the general MRL.

The general MRL of 0.1 ppm will apply for enforcement purposes with respect to the residues of trichlorfon in food for all commodities, including beef cattle and milk.

Environmental Considerations

What Happens When Trichlorfon is Introduced Into the Environment?

Trichlorfon poses a potential risk to certain terrestrial and aquatic organisms; therefore, additional risk-reduction measures must be observed.

Trichlorfon is not expected to persist in soil or aquatic environments. There is a high potential for mobility due to the very high solubility in water and weak adsorption to soil. Trichlorfon has a minimal potential for bioaccumulation. Dichlorvos is a major transformation product when trichlorfon decomposes in water.

The forestry use as well as the livestock and ornamental outdoor uses of trichlorfon are not expected to contaminate drinking water sources. In addition, the relatively short half-lives for dichlorvos and trichlorfon in surface water further decreases the potential for contamination of drinking water sources. Therefore, drinking water risks are not of concern.

Estimated environmental concentrations for water and land ecosystems were determined for the forestry and ornamental outdoor uses of trichlorfon based on the range of application rates and number of applications listed on the current labels of registered products. The uses on livestock were not expected to result in appreciable exposure to non-target organisms found on land and in the water; therefore, an assessment was not conducted for this use-pattern.

Birds, small wild mammals, bees and aquatic organisms such as fish and aquatic invertebrates can be affected when trichlorfon is used. To reduce exposure of these organisms, it is important that additional risk-reduction measures be observed.

Aerial application in forestry is of particular concern because the risk to pollinators, birds and small wild mammals cannot be mitigated. The buffer zones calculated for aerial application are large and believed to be operationally unfeasible. Therefore, aerial applications of trichlorfon are to be phased-out.

Value Considerations

What is the Value of Trichlorfon?

No additional information with respect to the value of trichlorfon was provided in response to the preliminary assessment published in Re-evaluation Note REV2007-05 or Proposed Re-evaluation Decision PRVD2008-14.

The registered chemical alternatives for unsupported uses of trichlorfon or for the supported uses of trichlorfon that have risk concerns are listed in Appendix V of PRVD2008-14.

Measures to Minimize Risk

The labels of registered pesticides include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law.

Risk-reduction measures are required to address potential risks that were identified in the assessment. These measures, in addition to those already on existing trichlorfon product labels, are designed to further protect human health and the environment. As a result of the re-evaluation of trichlorfon, the PMRA is requiring further risk-reduction measures on product labels.

Additional Key Risk-Reduction Measures

- As per the registrant's original agreement, all unsupported uses must be removed from the Dylox 80% Soluble Powder (Registration Number 9827) label and Dylox 420 Liquid Insecticide (Registration Number 16387) must be discontinued.

Human Health

- Label updates to the Toxicological Information section, which will provide information about symptoms and treatment for exposed individuals.
- Engineering controls (water-soluble packaging for soluble powder formulations), additional personal protective equipment, restricted-entry intervals and restrictions on number of applications to protect mixers/loaders/applicators and workers entering treated sites.
- Phase-out of residential use (municipal parks) and the use on outdoor ornamentals.

Environment

- Changes to label statements—including precautionary statements for bees, birds, small wild mammals and aquatic organisms as well as restrictions on field sprayer and airblast applications—to reduce release of trichlorfon into the environment.

- The observance of buffer zones to mitigate the entry of spray drift into aquatic systems.

- The phase-out of aerial applications of trichlorfon to protect aquatic habitats that may contain sensitive species.

Appendix I lists all the required label amendments.

What Additional Scientific Information is Being Requested?

The human health risks and/or risks to the environment for certain uses of trichlorfon were found to be acceptable and additional confirmatory scientific information is being requested from registrants as a result of this re-evaluation. Appendix II lists the additional data requirements.

Other Information

For trichlorfon, the summary of assessments found in PRVD2008-14 serves as an evaluation report. A list of references considered by the PMRA in support of the registration decision are found in this Re-evaluation Decision (Appendix III). The relevant test data on which the decision is based are available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa). For more information, please contact the PMRA's Pest Management Information Service by phone (1-800-267-6315) or by e-mail (pmra_infoserv@hc-sc.gc.ca).

Any person may file a notice of objection[5] regarding this decision on trichlorfon within 60 days from the date of publication of this Re-evaluation Decision. For more information regarding the basis for objecting (which must be based on scientific grounds), please refer to the PMRA's website (Request a Reconsideration of Decision, www.pmra-arla.gc.ca/english/pubreg/reconsideration-e.html), or contact the PMRA's Pest Management Information Service by phone (1-800-267-6315) or by e-mail (pmra_infoserv@hc-sc.gc.ca).

Once all organophosphate pesticides have been re-evaluated, a cumulative risk assessment will be conducted. The assessment will consider potential exposure to all chemicals causing toxicity in the same manner. The results of the cumulative risk assessment may affect any previous re-evaluation decision.

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[5] As per subsection 35(1) of the *Pest Control Products Act*.

Appendix I Label Amendments for Commercial and Restricted Class Products Containing Trichlorfon

Label Amendments Relating to Human Health
The use of water-soluble packets for soluble powder formulations is required to reduce exposure when mixing or loading the product. Canadian end-use product labels must be amended to include the following statements to further protect workers.

General (all)

Not to be used in conjunction with products containing naled or dichlorvos.

TOXICOLOGICAL INFORMATION:

Trichlorfon is an organophosphate that is a cholinesterase inhibitor. Typical symptoms of overexposure to cholinesterase inhibitors include headache, nausea, dizziness, sweating, salivation, runny nose and eyes. This may progress to muscle twitching, weakness, tremor, incoordination, vomiting, abdominal cramps and diarrhea in more serious poisonings. A life-threatening poisoning is signified by loss of consciousness, incontinence, convulsions and respiratory depression with a secondary cardiovascular component. Treat symptomatically. If exposed, plasma and red blood cell cholinesterase tests may indicate degree of exposure (baseline data are useful). Atropine, only by injection, is the preferable antidote. Oximes, such as pralidoxime chloride, may be therapeutic if used early; however, use only in conjunction with atropine. In cases of severe acute poisoning, use antidotes immediately after establishing an open airway and respiration. With oral exposure, the decision of whether to induce vomiting or not should be made by an attending physician.

For products that contain greater than 10% petroleum distillates, the following text must also be added to the Toxicological Information section (placed at the end of the paragraph presented above), as an additional aid to the attending physician.

NOTE: Product contains a petroleum distillate solvent.

Neguvon Pour-On Cattle Insecticide (Registration Number 9419)

Wear long, chemical-resistant gloves or gauntlets during use.

Wear chemical-resistant gloves when handling treated cattle.

Dylox 80% Soluble Powder (Registration Number 9827)

Wear coveralls over long-sleeved shirt and long pants during mixing, loading and application.

Wear respirator for high-pressure handwand and airblast applications.

Limit of 2 applications per year, 7 days apart.

REI of 10 days for Balsam fir and spruce trees in farm woodlots, rights-of-way, Christmas tree plantations.

Not for use in greenhouse or other enclosed areas.

Label Amendments Relating to the Environment
The following additional label statements are required to further protect the environment.

ENVIRONMENTAL HAZARDS

TOXIC to aquatic organisms, birds, and small wild mammals.

TOXIC to bees exposed to direct treatment, drift or residues on flowering crops or weeds. **DO NOT** apply this product to flowering crops or weeds if bees are visiting the treatment area. Minimize spray drift to reduce harmful effects on bees in habitats close to the application site.

DIRECTIONS FOR USE

Field sprayer application: **DO NOT** apply during periods of dead calm. Avoid application of this product when winds are gusty. **DO NOT** apply with spray droplets smaller than the American Society of Agricultural Engineers (ASAE) fine/medium/coarse classification. Boom height must be 60 cm or less above the crop or ground.

Airblast application: **DO NOT** apply during periods of dead calm. Avoid application of this product when winds are gusty. **DO NOT** direct spray above plants to be treated. Turn off outward pointing nozzles at row ends and outer rows. **DO NOT** apply when wind speed is greater than 16 km/h at the application site as measured outside of the treatment area on the upwind side.

DO NOT apply by air.

Buffer zones

The buffer zones specified in the table below are required between the point of direct application and the closest downwind edge of sensitive freshwater habitats (such as lakes, rivers, sloughs, ponds, prairie potholes, creeks, marshes, streams, reservoirs and wetlands) and estuarine/marine habitats.

Buffer Zones Required for the Protection of Aquatic Habitat Following Applications of Trichlorfon

Method of application	Crop	Buffer Zones (metres) Required for the Protection of			
		Freshwater Habitat of Depths:		Estuarine/Marine Habitats of Depths:	
		Less than 1 m	Greater than 1 m	Less than 1 m	Greater than 1 m
Airblast (early growth stage)	Forests, woodlots	50	40	50	40
Airblast (late growth stage)	Forests, woodlots	40	30	40	30

Appendix II Additional Data Requirements

The following confirmatory data are required to support the continued registration of trichlorfon.

DACO 6.2 The nature of the residue in livestock is not understood. Complete identification of metabolites is required to fully depict the metabolism in livestock.

DACO 7.6 (a) The registrant is required to explain the difference between the concentration of trichlorfon found in magnitude of residue study and that which was found in the nature of the residue study.

(b) The registrant is required to provide all available studies related to the magnitude of residues that may be incurred in milk.

References

A. Studies/Information Provided by the Applicant/Registrant (Unpublished)

Toxicology

Bond, G.P. 1986. Primary Dermal Irritation of Technical Trichlorfon in Albino Rabbits. Mobay Research. Report N°. 93005. June 4, 1986. DACO 4.2.5.

Hayes, R.H. 1988. Oncogenicity Study of Technical GradeTrichlorfon (DYLOX) with Mice. Study N°. 85-271-01. July 28, 1988. DACO 4.4.2

Kowalski, R.L. et al. 1987. A Teratology Study with Dylox® Technical (Trichlorfon) in the Rat. Miles Laboratories, Inc., Elkhart, IN. Mobay Report N°. 94638, Laboratory Report N°. MTD0017. DACO 4.5.2.

Sheets, L.P. 2003. A Developmental Neurotoxicity Screening Study with Technical Grade Trichlorfon. Bayer CropScience LP, Stilwell, Kansas. Study N°. 01-D72-CT. February 26, 2003. DACO 4.5.14.

Residue Chemistry

Auer, S., and R. Krebber. 1998. Determination of Residues of Trichlorfon and Dichlorvos in Edible Tissues (Muscle, Fat, Kidney and Liver) 12 Hours to 7 Days after a Single Spray Treatment on Cattle.Bayer Inc., Agriculture Division. 119 p.

Chopade, H.M., L.L. Bosnak, and M. B. Lasley. 30 June 1987. Distribution and metabolism of Dylox in lactating goats. Bayer Inc., Agriculture Division. 156 p.

Krebber, R. 1998. Determination of Storage Stability of Trichlorfon and Dichlorvos in Tissues of Cattle. Bayer Inc., Agriculture Division. 61 p.

Krebber, R. 1998. Method for the HPLC/MS/MS Determination of Trichlorfon and Dichlorvos in Cattle Tissue. Bayer Inc., Agriculture Division. 25 p

Lynch, C. J. and G.C. Speirs. 1998. [Ethyl-1-^{14}C]-Trichlorfon: Total Residue Depletion Study in Cattle after Dermal Application (In-Life Phase). Bayer Inc., Agriculture Division. 46 p.

Phillips, M. and S. Johnson. 1998. [Ethyl-1-^{14}C]-Trichlorfon: Investigation of the Nature of Metabolites in Edible Tissues of Cattle after Dermal Application (Animals 1 male and 2 female). Inveresk Research, Scotland. 226 p.

Occupational

Armstrong, T.F. 1998a. Determination of Transferable Turf Residues on Turf Treated with Dichlorvos in California. Study N°. 98ABG01. Agri Business Group Inc.

Armstrong, T.F. 1998b. Determination of Transferable Turf Residues on Turf Treated with Dichlorvos in Florida. Study N°. 98ABG02. Agri Business Group Inc.

Armstrong, T.F. 1998c. Determination of Transferable Turf Residues on Turf Treated with Dichlorvos in Ontario, Canada. Study N°. 98ABG03. Agri Business Group Inc.

B. Additional Information Considered for Trichlorfon Re-evaluation (Published Information)

Toxicology

Becker, R.E., J. Colliver, R. Elble, E. Feldman, E. Giacobini, V. Kumar, S. Markwell, P. Moriearty, P. Parks, S.D. Shillcut, L. Unni, S. Vicari, C. Womack, and R.F. Zec. 1990. Effects of metrifonate, a long-acting cholinesterase inhibitor in Alzheimer Disease: Report of an open trial. *Drug Development Research* 19: 425- 434.

Berge, G.N. et al. 1986. Prenatal Effects of Trichlorfon on the Guinea Pig Brain. *Archives of Toxicology*. 59:30-35.

Berge, G.N. et al. 1987. Neurotoxic Effects of Prenatal Trichlorfon Administration in Pigs. *Acta. Vet. Scand.* 28(3-4): 321-32.

California Environmental Protection Agency. 1999. Summary of Toxicology Data - Trichlorfon, Chemical Code: 88, Tolerance 98 SB 950 #: 014, California Environmental Protection Agency, Department of Pesticide Regulation, Medical Toxicology Branch, First Draft: March 9, 1997, Updated: January 6, 1999.

Cummings, J.L. et al. 1998. Metrifonate Treatment of the Cognitive Deficits of Alzheimer's Disease. *Neurology,* 50:1214-1221.

Cutler et al. 1998. Safety and Tolerability of Metrifonate in Patients with Alzheimer's Disease:Results of a Maximum Tolerated Dose Study. *Life Sciences*, 62(16):1433-1441.

Czeizel, A.E. et al. 1993. Environmental trichlorfon and cluster of congenital abnormalitites. *The Lancet*, 341:539-542.

Czeizel, A.E. 1994. Phenotypic and cytogenetic studies in self-poisoned patients. *Mutation Research*, 313:175-181.

EPA.1999. Memorandum. Abdallah Khasawinah, Reregistration Branch 4 Health Effects Division, Office of Prevention, Pesticides and Toxic Substances. Subject: Trichlorfon; Chemical N°. 057901. The HED Toxicology Chapter for the Risk Assessment for the Reregistation Eligibility Decision Document (RED), Case #0104. August 9, 1999.

EPA. 1999. Memorandum . Jess Rowland and Pauline Wagner, Hazard Identification Assessment Review Committee, Health Effects Division to W. Phang, Reregistration Branch 1,

Health Effects Division. Subject: Trichlorfon - Replacement of Human Study Used in Risk Assessments - Report of the Hazard Identification Assessment Review Committee. June 2, 1999.

EPA. 2000. Memorandum.Thurston Morton, Reregistration Branch 4, Health Effects Division to Kylie Rothwell Reregistration Section , Special Review and Reregistration Division. Subject: Trichlorfon: Chemical N°. 057901. HED's Revised Preliminary Human Health Risk Assessment for Trichlorfon. April 18, 2000.

Hayes, W.J. Jr. 1982. Pesticides Studied in Man. Baltimore, Maryland, Williams & Wilkins Co., pp. 351-356.

Hinz, V.C. et al. 1996. Metrifonate and Dichlorvos: Effects of a Single Oral Administration on Cholinesterase Activity in Rat Brain and Blood. *Neurochemical Research*. 21(3):339-345.

Hinz, V.C. et al. 1998. Effects of Subchronic Administration of Metrifonate on Cholinergic Neurotransmission in Rats. *Neurochemical Research* 23(7):931-938.

Johnson, M.K. 1981. Delayed neurotoxicity - do trichlorfon and/or dichlorvos cause delayed neuropathy in man or in test animals? *Acta pharmacol. toxicol.* 49(Suppl. V): 87-98.

Joint FAO/WHO Meeting on Pesticide Residues .1971. WHO Pesticide Residues Series 1: Trichlorfon.

Joint FAO/WHO Meeting on Pesticide Residues. 1975. WHO Pesticide Residues Series 5: Trichlorfon.

Joint FAO/WHO Meeting on Pesticide Residues. 1978. Pesticide Residues in Food: Trichlorfon.

Knox, B. et al. 1978. Congenital Ataxia and Tremor with Cerebellar Hypoplasia in Piglets Borne by Sows Treated with Neguvon® vet. (Metrifonate, Trichlorfon) during Pregnancy. *Nord. Vet.-Med.* 30:538-545.

McKeith, I.G. 1998. The Clinical Trial Protocol of the Metrifonate in Alzheimer's Trial (MALT). *Dementia and Geriatric Cognitive Disorders* 9(Suppl 2):2-7.

Monson, M.H., and K. Alexander. 1984. Metrifonate in pregnancy. *Transactions of the Royal Society of Tropical Medecine and Hygiene* 78: 565.

Morris, J.C. et al. 1998. Metrifonate Benefits Cognitive, Behavioral, and Global Function in Patients with Alzheimer's Disease. *Neurology*, 50:1222-1230

Pettigrew, L.C. et al. 1998. Pharmacokinetics, Pharmacodynamics and Safety of Metrifonate in Patients with Alzheimer's Disease. *Journal of Clinical Pharmacology* 38:236-245.

Unni, L.K. et al. 1994. Pharmacokinetics and Pharmacodynamics of Metrifonate in Humans. *Methods and Findings in Experimental and Clinical Pharmacology* 16(4):285-289.

WHO. 1991. Trichlorfon Health and Safety Guide, IPCS International Programme on Chemical Safety, Health and Safety Guide No. 66. World Health Organization, Geneva, 1991.

WHO. 1992. Environmental Health Criteria 132: Trichlorfon, World Health Organization, Geneva.

Residue Chemistry

Australian Pesticides and Veterinary Medecines Authority. 2004. PUBCRIS Registered Products Database. www.apvma.gov.au/pubcris/subpage_pubcris.shtml.

Agricultural Compounds and Veterinary Medicines. 2004. Database of currently registered veterinary medicines and plant compounds.
www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm.

EPA. January 1997. Trichlorfon Reregistration Eligibility Document (RED).

WHO. 2001. *Evaluation of certain veterinary drug residues in food.* WHO technical report series 900.

Occupational

Cooper R.J, Clark, J.M, Murphy, K.C. 1995. Volatilization and Dislodgeable Residues Are Important Avenues of Pesticide Fate. USGA Green Section Record. University of Massachusetts at Amherst.

EPA. 2000a. HED's Revised Preliminary Human Health Risk Assessment for Dichlorvos, Case # 0104. DP Barcode: D267106. Chemical No. 057901.

EPA. 2001. Report on FQPA Tolerance Reassessment Progress and Interim Risk Management Decision (TRED) for Trichlorfon. EPA 738-R-01-009. Case # 0104.

Murphy, K.C., R.J. Cooper, and J.M. Clark. 1996. Volatile and dislodgeable residues following trichlorfon and isazofos application to turfgrass and implications for human exposure. *Crop Science* 36(6): 1446-1454.

Ontario Cattlemen's Association. 2003. Average Carcass Weights - Federal and Provincial Inspected Packing Plants. Industry Statistics 2003. http://cattle.guelph.on.ca/statistics/

Statistics Canada. 2001. *Record levels of hogs and cattle.*
http://www.statcan.ca/english/agcensus2001/first/farmop/03livestock.htm. Accessed December 1, 2004 (last updated 2003-12-02).

Environment

Atkins, E.L., D. Kellum, and K.W. Atkins. 1981. *Reducing pesticide hazards to honey bees: Mortality prediction techniques and integrated management strategies*. University of California, Division of Agricultural Science, Leaflet 2883. 22 pp.

British Crop Protection Council. 1998. *Trichlorfon*. The Electronic Pesticide Manual.

Cohen, S.Z., S.M. Creeger, R.F. Carsel and C.G. Enfield. 1984. Potential for pesticide contamination of groundwater resulting from agricultural uses. Pages 297-325 In: R.F. Krugger and J.N. Seiber (eds.), *Treatment and Disposal of Pesticide Wastes*. ACS Symposium Series No. 259. American Chemical Society, Washington, DC, pp. 297-325.

Croft, B.A. and A.W.A. Brown. 1975. Responses of Arthropod Natural Enemies to Insecticides, *Arthropod Natural Enemies and Insecticides.* Article 6799 of Michigan State University Agricultural Experiment Station, Michigan State University, East Lansing. 336 pp.

Delahaut, K. and C.F. Koval. 2001. *Earthworms: Beneficials or Pests?* University of Wisconsin Urban Horticulture Website.

EPA. 2000. Preliminary Risk Assessments of Dichlorvos.

EPA. 1997. Environmental Fate and Effects Division Re-Registration Eligibility Decision Document (EPA 738-R-96-017)

EPA. 2000. Standard Operating Procedure (SOP) For Standard Operating Procedure (SOP) For Incorporating Screening-Level Incorporating Screening-Level Estimates Of Drinking Water Exposure Estimates Of Drinking Water Exposure Into Aggregate Risk Assessments Into Aggregate Risk Assessments. Public Comment Draft.

Fletcher, J.S., J.E. Nellessen, and T.G. Pfleeger. 1994. Literature review and evaluation of the EPA food-chain (Kenaga) nomogram, an instrument for estimating pesticide residues on plants. *Environmental Toxicology and Chemistry* 13: 1383-1391.

Ganzelmeier, H., D. Rautmann, R. Spangenberg, M. Streloke, M. Herrmann, H.-J. Wenzelburger, and H.-F. Walter. 1995. *Studies on the spray drift of plant protection products: Results of a test program carried out throughout the Federal Republic of Germany*. Report Number 305 from the Biologischen Bundesanstalt fur Land - und Forstwirtschaft, Berlin-Dahlem. Blackwell Wissenschafts-Verlag GmbH, Berlin/Vienna.

Goring, C.A.I., D.A. Laskowski, J.H. Hamaker, and R.W. Meikle. 1975. Principles of pesticide degradation in soil. Pages 135-172 In : R. Haque and V.H. Freed (eds.) *Environmental dynamics of pesticides*. Plenum Press, New York.

Government of Canada. 1995. *Toxic Substances Management Policy, Persistence and Bioaccumulation Criteria*. Minister of Supply and Services, Ottawa, Ontario (ISBN 0-662-23524-X; Catalogue No. En 40-499/2-1995E).

Harris L.E. 1975. Guide for Estimating Toxic Residues in Animal Feeds or Diets. United States Environmental Protection Agency, Washington, Report EPA/540/9-75-019

Hoerger, F. and E.E. Kenaga. 1972. Pesticide Residues on Plants: Correlation of Representative Data as Basis for Estimation of Their Magnitude in the Environment. *In*: Coulston, F. and F. Korte (eds.) *Global Aspects of Chemistry, Toxicology and Technology as Applied to the Environment*, Volume I. Thieme, Stuttgart, and Academic Press, New York. pp. 9-28.

Jacques Whitford Environment Limited. 2001. Aquatic Monitoring Balsam Fir Sawfly 1999 Control Program, JWEL Project 1335, St. John's, Newfoundland. 119 pp.

Kenaga, E.E. 1973. Factors to be Considered in the Evaluation of the Toxicity of Pesticides to Birds in Their Environment. *In*: Coulston, F. and F. Korte (eds.) *Global Aspects of Chemistry, Toxicology and Technology as Applied to the Environment*, Volume II. Thieme, Stuttgart, and Academic Press, New York. pp. 166-181.

Lartiges, S.B., and P.P. Garrigues. 1995. Degradation Kinetics of Organophosphorus and Organonitrogen Pesticides in Different Waters under Various Environmental Conditions. *Environmental Science and Technology* 29:1246-1254.

McCall, J.P., D.A. Laskowski, R.L. Swann, and H.J. Dishburger. 1981. Measurement of sorption coefficients of organic chemicals and their use in environmental fate analysis. Pages 89-109 *In: Test protocols for environmental fate and movement of toxicants*. Proceedings of a symposium. Association of Official Analytical Chemists. 94th Annual Meeting, October 21-22, 1980. Washington, DC.

Mineau, P. 2002. Estimating the probability of bird mortality from pesticide sprays on the basis of the field study record. *Environmental Toxicology and Chemistry*. 21(7):1497-1506.

NRA. 2000. Section 7, Environmental Assessment Report, The NRA Review of Dichlorvos, National Registration Authority for Agricultural and Veterinary Chemicals, Australia, 2000.

Potter D.A., M.C. Buxton, C.T. Redmond, C.G. Patterson, and A.J. Powell. 1990. Toxicity of Pesticides to Earthworms (*Oligochaeta: Lumbricidae*) and Effect on Thatch Degradation in Kentucky Bluegrass Turf. *Journal of Economic Entomology* 83(6): 2362-2369.

Spector W.S. 1956. *Handbook of Biological Data*. W.B. Saunders, Philadelphia, p. 78, p. 187.

Townsend L., D. Potter, and A.J. Powell. 2001. *Earthworms: Thatch-Busters*. University of Kentucky Entomology Department.

United Nations Environment Programme. 1983. Trichlorfon, 33. N.F. Izmerov (ed.), International Register of Potentially Toxic Chemicals, USSR State Committee for Science and Technology, & USSR Commission for UNEP, Centre for International Projects, Moscow, 1983. 24 pp.

WHO. 1992. Trichlorfon, Environmental Health Criteria 132, The Environmental Health Criteria Series, World Health Organization, Geneva.

Willis G.H. and L.L. McDowell. 1987. Pesticide persistence on foliage. *Reviews of Environmental Contamination and Toxicology* 100: 23-69.

Wolf, T.M. and B.C. Caldwell. 2001. Development of a Canadian spray drift model for the determination of buffer zone distances. Page 60. *In: Expert Committee on Weeds - Comité d'experts en malherbologie (ECW-CEM)*. Proceedings of the 2001 National Meeting, Québec City. Saint-Anne-de-Bellevue, Québec: ECW-CEM. Eds. D. Bernier, D.R.A. Campbell and D. Cloutier.

Use Analysis

Bennett, K. (date unknown). *Caterpillar pests of cole crops in home gardens*. http://www.extension.umn.edu/yardandgarden/ygbriefs/e253caterpillarpests-cole.html

British Columbia Ministry of Agriculture and Lands. 2005. *Berry Production Guide 2005-2006.*

Howard, R.J., J.A. Garland, and W.L. Seaman. 1994. *Diseases and Pests of Vegetable Crops in Canada*. The Canadian Phytopathological Society and the Entomological Society of Canada.

Martin, R. 1988. *Intercropping to reduce European corn borer damage*. From website: http://www.eap.mcgill.ca/magrack/sf/Summer%2088%20C.htm

Park, S.J. 1985. *Growing field beans in Canada*. Agriculture and Agri-Food Canada, Publication 1787E.

Soroka, J.J. 1971. *Insect Pests of Legume and Grass Crops in Western Canada*. Agriculture and Agri-Food Canada, Publication 1435E.

University of California. 1992. *Integrated Pest Management for Cole Crops and Lettuce*. Publication 3307. University of California IPM Publications.